

L35 ANSWER 203 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:106808 HCAPLUS Full-text
DOCUMENT NUMBER: 116:106808
TITLE: Preparation of immunosuppressive cyclosporin A analogs
with modified amino acids at position 8
INVENTOR(S): Patchett, Arthur A.; Taub, David; Goegelman, Robert T.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 444897	A1	19910904	EP 1991-301581	19910227
R: CH, DE, FR, GB, IT, LI, NL				
US 5122511	A	19920616	US 1990-485920	19900227
CA 2036963	AA	19910828	CA 1991-2036963	19910225
JP 04211699	A2	19920803	JP 1991-32626	19910227
US 5214130	A	19930525	US 1991-744039	19910812
			US 1990-485920	A 19900227

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 116:106808

GI For diagram(s), see printed CA Issue.

AB Title compds. I [Y = NHC:CH₂CO, NHCHCH₂RCO; R = Me(OCH₂CH₂)_nS(O)_m; RaS(O)_m; m = 0,1; n = 1-4; Ra = H when m = 0, (substituted) C₁-6 alkyl, (substituted) Ph, (substituted) CH₂Ph, Q, Q₁; R₁ = N-methyl-(4R)-4-[(E)-2- butenyl]-4-methyl-L-threonine or its 3-desoxy or dihydro equivalent; R₂ = L-α-aminobutyric acid, Ala, Nva, Ser, Thr, Val; R₃ = sarcosinyl, N-methyl-D-alanyl; R₄, R₆, R₉, R₁₀ = MeLeu, MeVal; R₅ = Val, Nva; R₇ = Ala, L-α-aminobutyric acid, Phe; R₁₁ = MeVal, D-MeVal, MeNva] were prepared as immunosuppressives and antiinflammatories. Thus, [2-deutero-3-fluoro-D-Ala]8-cyclosporin A (preparation via fermentation of Tolypocladium inflatum culture given) was treated with LDA to give [dehydro-Ala]8-cyclosporin A. This was active against T-cell proliferation from mouse spleen cells.

IT 139123-37-8P 139123-38-9P 139123-39-0P
139123-40-3P 139123-41-4P 139123-42-5P
139123-43-6P 139123-44-7P 139123-45-8P
139123-46-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

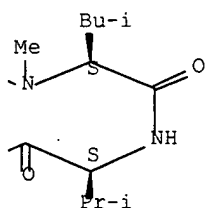
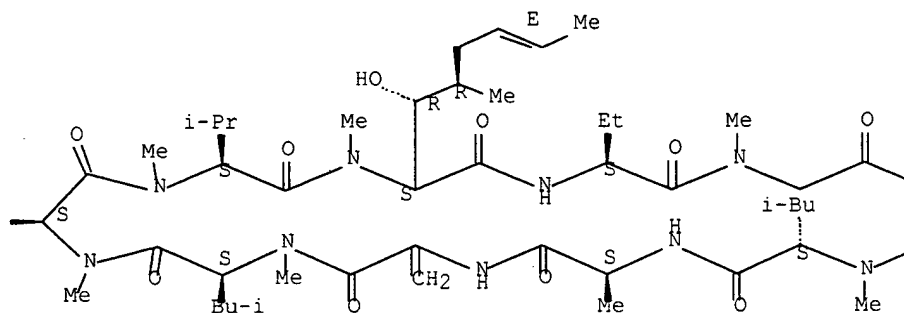
(preparation of, as immunosuppressive and antiinflammatory agent)

RN 139123-37-8 HCAPLUS

CN Cyclosporin A, 2-(2,3-didehydroalanine)- (9CI) (CA INDEX NAME)

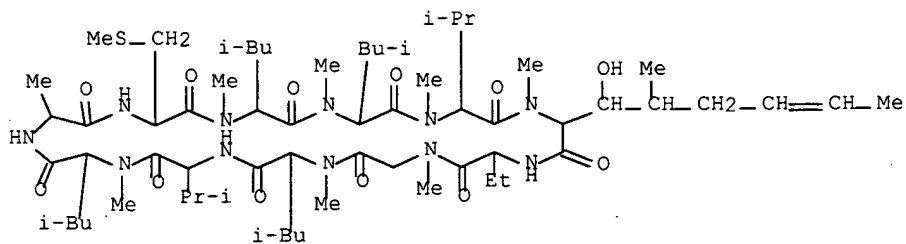
Absolute stereochemistry.

Double bond geometry as shown.



RN 139123-38-9 HCAPLUS

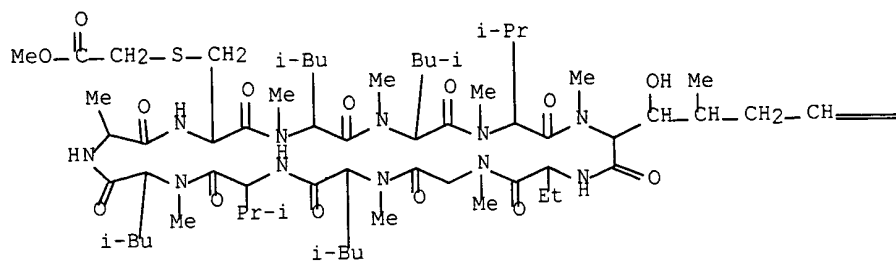
CN Cyclosporin A, 2-(S-methyl-D-cysteine)- (9CI) (CA INDEX NAME)



RN 139123-39-0 HCAPLUS

CN Cyclosporin A, 2-[S-(2-methoxy-2-oxoethyl)-D-cysteine]- (9CI) (CA INDEX NAME)

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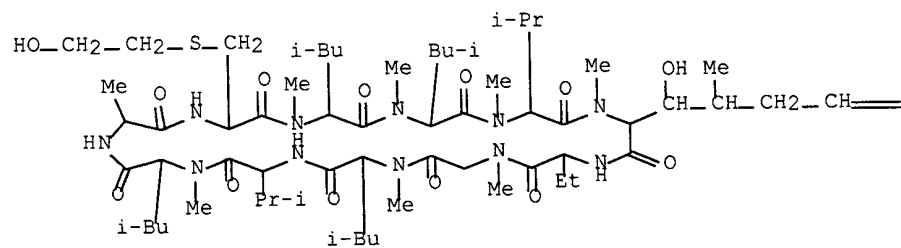


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= CH₂ Me

RN 139123-40-3 HCAPLUS
 CN Cyclosporin A, 2-[S-(2-hydroxyethyl)-D-cysteine]- (9CI) (CA INDEX NAME)

PAGE 1-A

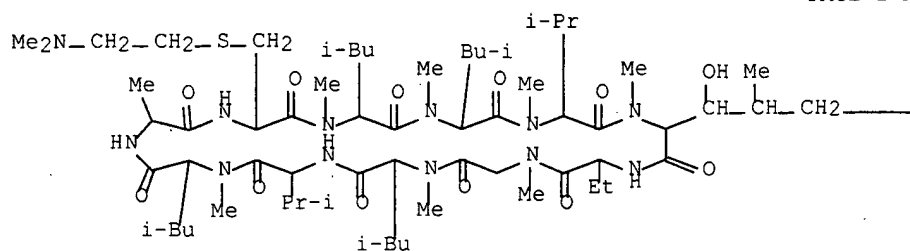


PAGE 1-B

= CH₂ Me

RN 139123-41-4 HCAPLUS
 CN Cyclosporin A, 2-[S-[2-(dimethylamino)ethyl]-D-cysteine]- (9CI) (CA INDEX NAME)

PAGE 1-A

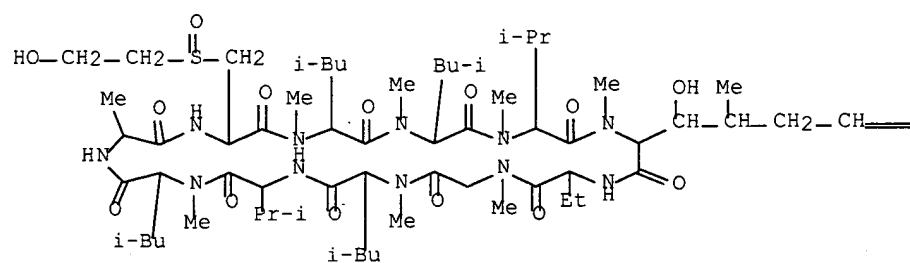


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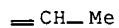


RN 139123-42-5 HCAPLUS
 CN Cyclosporin A, 2-[3-[(2-hydroxyethyl)sulfinyl]-D-alanine]- (9CI) (CA INDEX NAME)

PAGE 1-A

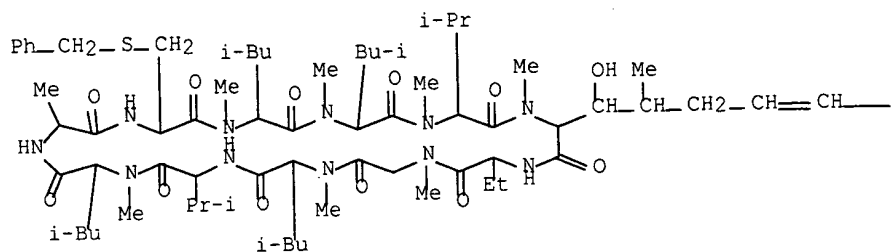


PAGE 1-B



RN 139123-43-6 HCAPLUS
 CN Cyclosporin A, 2-[S-(phenylmethyl)-D-cysteine]- (9CI) (CA INDEX NAME)

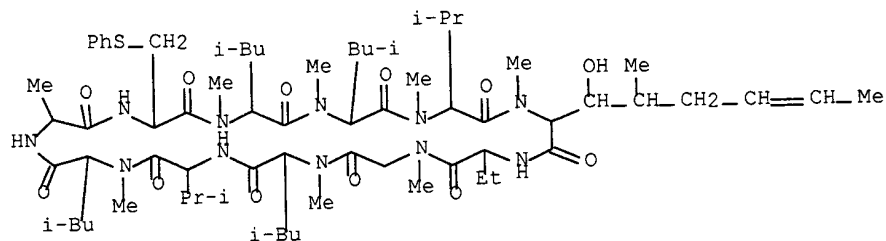
PAGE 1-A



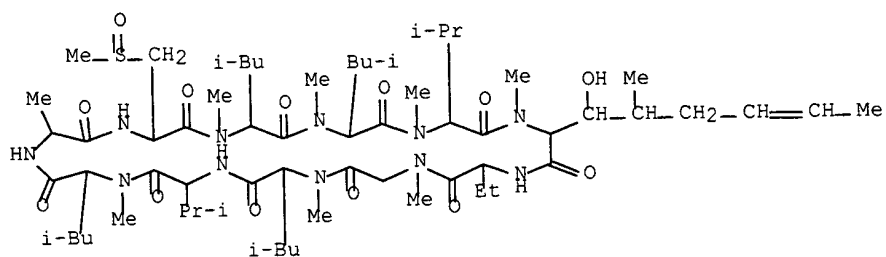
PAGE 1-B

— Me

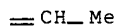
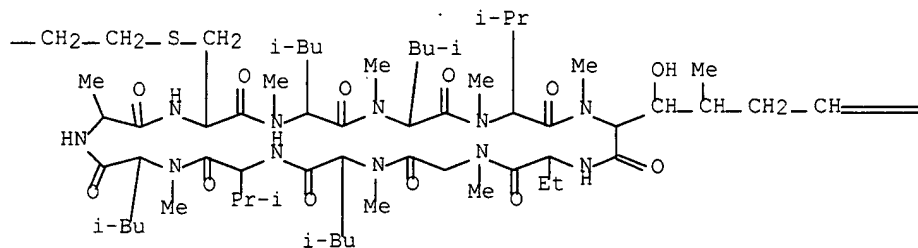
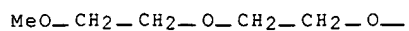
RN 139123-44-7 HCAPLUS
CN Cyclosporin A, 2-(S-phenyl-D-cysteine)- (9CI) (CA INDEX NAME)



RN 139123-45-8 HCAPLUS
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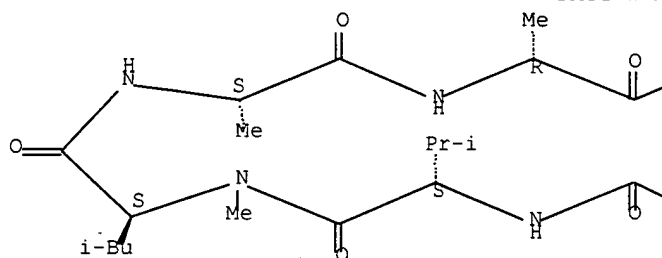


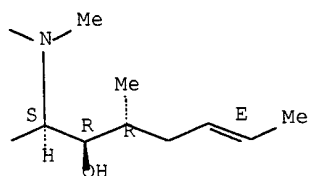
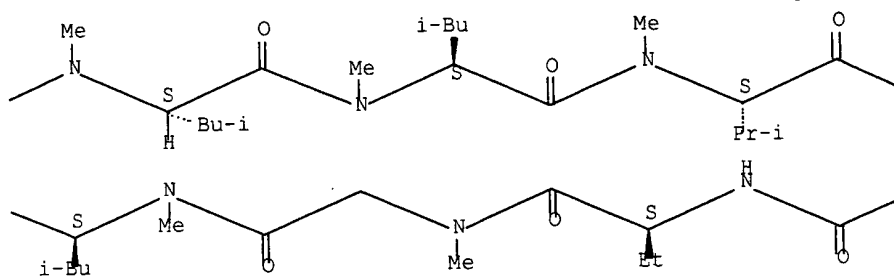
RN 139123-46-9 HCAPLUS
CN Cyclosporin A, 2-[S-[2-[2-(2-methoxyethoxy)ethoxy]ethyl]-D-cysteine]- (9CI) (CA INDEX NAME)



IT 59865-13-3DP, Cyclosporin A, analogs
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as immunosuppressives and antiinflammatories)
 RN 59865-13-3 HCAPLUS
 CN Cyclosporin A (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.





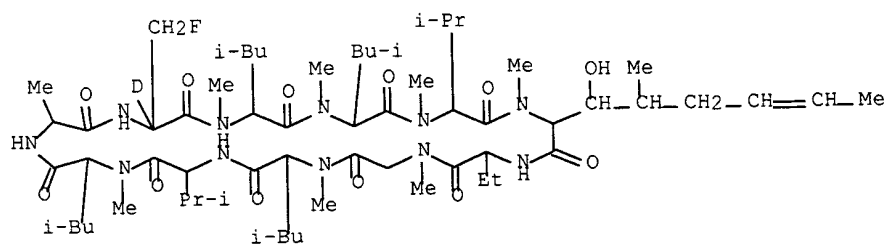
IT 139123-47-0P 139123-48-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for immunosuppressives and antiinflammatories)

RN 139123-47-0 HCAPLUS

CN Cyclosporin A, 2-(3-fluoro-D-alanine-2-d)- (9CI) (CA INDEX NAME)



RN 139123-48-1 HCAPLUS

CN Cyclosporin A, 2-(3-fluoro-D-alanine)- (9CI) (CA INDEX NAME)

